General

Guideline Title

Human immunodeficiency virus type 2 (HIV-2).

Bibliographic Source(s)

New York State Department of Health. Human immunodeficiency virus type 2 (HIV-2). New York (NY): New York State Department of Health; 2012 Apr. 14 p. [44 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The quality of evidence (I-III) and strength of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Introduction

Key Points:

- Human immunodeficiency virus (HIV)-2-infected individuals with progressive disease are less likely to respond as predictably to antiretroviral therapy (ART) as patients with HIV-1 infection.
- The choice of ART for HIV-2 differs from that for HIV-1, underscoring the importance of differentiating between HIV-1 and HIV-2 in patients at risk for HIV-2 infection.
- Clinical monitoring of HIV-2 is hampered by the absence of assays with Food and Drug Administration (FDA) approval for quantification of HIV-2 viral load, as well as a lack of consensus on interpretation of HIV-2 resistance testing.

HIV-2 Screening and Diagnosis

Specimens submitted for HIV testing should be screened by an enzyme immunoassay (EIA) that detects HIV-1, HIV-1 group O, and HIV-2. All laboratories performing HIV diagnostic testing should incorporate algorithms for differentiation of HIV-1 versus HIV-2 in repeatedly reactive samples (see the National Guideline Clearinghouse [NGC] summary of the New York State Department of Health [NYSDoH] guideline Diagnostic, Monitoring, and Resistance Laboratory Tests for HIV). (AIII)

When HIV-1/HIV-2 combination screening yields a reactive result but is followed by indeterminate or nonreactive HIV-1 Western blot, clinicians should:

- Obtain a plasma HIV ribonucleic acid (RNA) assay to exclude acute HIV-1 infection (AIII)
- Obtain testing for HIV-2 antibodies with an FDA-approved HIV-1/HIV-2 type-differentiating immunoassay if acute HIV-1 infection has been excluded (AIII)
- Consider specimens positive for HIV-2 if they are repeatedly reactive on an HIV-1/HIV-2 screening test and reactive for HIV-2 antibodies on the HIV-1/HIV-2 differentiation test (AIII)

Clinicians should use HIV-1/HIV-2 type-differentiating immunoassays and nucleic acid testing protocols when screening for HIV in patients who meet the criteria outlined in the Table below. (AIII)

Table. Patients Who Should Receive Testing That Differentiates HIV-1 and HIV-2

Clinicians should be alert to the possibility of HIV-2 infection in patients who: • Originated in or have traveled to an HIV-2-endemic area[a] • Received medical care, injections, immunizations, phlebotomy, surgery, or blood products or participated in vaccine trials in an HIV-2-endemic area[a] • Had sexual or needle-sharing contact with persons who are infected with HIV-2 or are from an HIV-2-endemic area[a] • Were born to a mother with HIV-2 infection[b] • Had opportunistic infections or other clinical symptoms of HIV/AIDS but tested negative or indeterminate for HIV-1 • Received multiple HIV-1 indeterminate antibody test results • Have a confirmed diagnosis of HIV-1 but an undetectable viral load that is incompatible with the clinical or immunological status
[a]HIV-2 endemic areas include West African countries (Guinea-Bissau, Cape Verde, Ivory Coast, Gambia, Mali, Mauritania, Nigeria, Sierra Leone, Benin, Burkina Faso, Ghana, Guinea, Liberia, Niger, Sao Tome, Senegal, and Togo), as well as Angola, Mozambique, and India. [b]See "Testing and Prophylaxis for HIV-2-Exposed Infants" subsection in the "HIV-2 and Pregnancy" section below.

For additional information regarding HIV-1/HIV-2 combination rapid tests, see the NGC summary of the NYSDoH guideline Diagnostic, Monitoring, and Resistance Laboratory Tests for HIV (Table 2. Characteristics of FDA-Approved Rapid HIV Tests).

Key Point:

Diagnostic HIV laboratory tests and interpretation algorithms evolve; individual laboratories have internal protocols for reporting tests with preliminary results. *Indeterminate*, *inconclusive*, *non-diagnostic*, and *pending validation* are among the terms used when preliminary results cannot be classified definitively. The clinician should contact the appropriate laboratory authority to determine the significance of the non-definitive results and the supplemental testing that would be indicated. This is of particular importance in tests from patients with suspected HIV-2 infection. Clinicians should become familiar with the internal test-reporting policies of their institutions.

Refer to the original guideline document for the list of public health laboratories for New York City and New York State providers.

HIV-2 Disease Monitoring

Clinicians should monitor HIV-2-infected patients by clinical evaluation and CD4 cell count. (BIII)

HIV-2 Treatment

Clinicians should include two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and an appropriate boosted protease inhibitor (PI), such as lopinavir, saquinavir, or darunavir, when prescribing ART for HIV-2 mono-infected or HIV-1/HIV-2 co-infected individuals (see Table 2 in the original guideline document). (AIII)

Clinicians should *not* prescribe non-nucleoside reverse transcriptase inhibitors (NNRTIs) or the PIs nelfinavir, atazanavir, or fosamprenavir as part

of an ART regimen against HIV-2 mono-infection; these agents may be used as part of a regimen for HIV-1/HIV-2 co-infected patients if adequate treatment for HIV-2 is also included (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2011). (BIII)

Clinicians should consult with a provider with experience in the management of HIV-2 before initiating ART in HIV-2-infected patients. (AIII)

Clinicians should educate patients with confirmed HIV-2 infection about the lack of data regarding treatment of HIV-2 and should review individual benefits and risks of initiating treatment. Patients should make the final decision of whether and when to initiate ART.

Key Point:

Few data exist for the diagnosis and management of HIV-1/HIV-2 co-infection; however, clinical management currently focuses on controlling HIV-1 infection with agents that are active against both HIV-1 and HIV-2.

HIV-2 and Pregnancy

Clinicians caring for pregnant patients with suspected or diagnosed HIV-2 should consult with a provider with experience in HIV-2 testing and management, including perinatal ART for HIV-2-infected pregnant women and postnatal ART for HIV-2-exposed infants. (AIII)

HIV-2 Testing for Women during Pregnancy and Delivery

Clinicians should use HIV-1/HIV-2 type-differentiating immunoassays and nucleic acid testing protocols when screening for HIV in pregnant women who meet the criteria outlined in the Table above. (AIII)

For more information regarding HIV testing during pregnancy, refer to the NGC summary of the NYSDoH guideline HIV Testing during Pregnancy and at Delivery.

HIV-2 Treatment and Prophylaxis during Pregnancy

Zidovudine plus lamivudine with lopinavir/ritonavir is the currently recommended regimen for HIV-2-infected pregnant women. (AIII) For HIV-2-infected women who decline ART or who are unable to adhere to an ART regimen during pregnancy, single-drug prophylaxis with zidovudine during pregnancy and intrapartum should be used as an alternative for preventing HIV-2 mother-to-child transmission (MTCT). (BIII)

For additional information regarding prescribing ART for pregnant women, refer to the NGC summary of the NYSDoH guideline Antiretroviral Therapy and *Use of ART in HIV-Infected Pregnant Women*.

Testing and Prophylaxis for HIV-2-Exposed Infants

All infants born to mothers infected with HIV-2 should receive the standard 6-week zidovudine prophylactic regimen (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2011; de Ruiter et al., 2008). (AIII)

Clinicians should advise HIV-2-infected women about the risk of postpartum MTCT via breast milk. Breastfeeding is contraindicated for both HIV-1- and HIV-2-infected mothers, even when receiving ART. (AI)

The NYSDoH strongly recommends that all New York State birth facilities use the pediatric HIV testing services at the Wadsworth Center (see the NYSDoH guideline Diagnosis of Pediatric HIV Infection in HIV-Exposed Infants for the recommended diagnostic testing schedule).

Definitions:

Quality of Evidence for Recommendation

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Clinical Algorithm(s)

An alternative diagnostic algorithm for HIV diagnosis is provided in the original guideline document.

Scope

Disease/Condition(s)

- Human immunodeficiency virus type 2 (HIV-2) infection
- HIV-1/HIV-2 co-infection

Guideline Category

Counseling

Diagnosis

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Allergy and Immunology

Family Practice

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

Pediatrics

Pharmacology

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To provide guidelines for the diagnosis and management of patients with suspected human immunodeficiency virus type 2 (HIV-2) infection or HIV-1/HIV-2 co-infection

Target Population

Patients with suspected or diagnosed human immunodeficiency virus type 2 (HIV-2) infection or HIV-1/HIV-2 co-infection including pregnant women and HIV-2-exposed infants

Interventions and Practices Considered

Screening/Diagnosis/Evaluation/Risk Assessment

1. Human immunodeficiency virus (HIV) testing by an enzyme immunoassay (EIA) that detects HIV-1, HIV-1 group O, and HIV-2
2. Plasma HIV ribonucleic acid (RNA) assay to exclude acute HIV-1 infection
3. Testing for HIV-2 antibodies with HIV-1/HIV-2 type-differentiating immunoassay if acute HIV-1 infection has been excluded
4. Screening patients for HIV-2 infection based on established criteria
5. Monitoring HIV-2-infected patients by clinical evaluation and CD4 cell count

Treatment/Management

1. Use of two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and a boosted protease inhibitor (PI), such as lopinavir, saquinavir, or darunavir, for HIV-2 mono-infection or HIV-1/HIV-2 co-infection
2. Avoiding use of non-nucleoside reverse transcriptase inhibitors (NNRTIs) or the PIs nelfinavir, atazanavir, or fosamprenavir as part of a regimen against HIV-2 mono-infection
3. Consultation with a provider with experience in the management of HIV-2 before initiating antiretroviral therapy in HIV-2-infected patients
4. HIV-2 patient education on risk and benefits of treatment
5. Consultation with providers familiar with HIV-2 infection in pregnancy and during the post-natal period
6. Use of HIV-1/HIV-2 type-differentiating immunoassays and nucleic acid testing protocols when screening for HIV in pregnant women who meet criteria for HIV-2 infection
7. Use of the zidovudine plus lamivudine with lopinavir/ritonavir regimen for HIV-2-infected pregnant women
8. Use of 6-week zidovudine prophylactic regimen in infants born to HIV-2-infected mothers
9. Advising HIV-2-infected women about the risk of postpartum mother-to-child transmission via breast milk

Major Outcomes Considered

- Incidence of human immunodeficiency virus (HIV)-2 mono-infection and HIV-1/HIV-2 co-infection
- Accuracy of diagnostic and screening tests
- Risk of mother-to-child transmission of HIV-2
- Efficacy of antiretroviral therapy against HIV-2 infection

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

MEDLINE was searched up to April 2012 with use of appropriate key words. Due to lack of randomized controlled trials on this subject, evidence is limited to qualitative studies, reviews, and case reports. Antiretroviral therapy and perinatal transmission guidelines from the Department of Health and Human Services were reviewed, as well as guidelines from the British Human Immunodeficiency Virus (HIV) Association. Surveillance data and protocols from the New York City Department of Health and Mental Hygiene and Centers for Disease Control and Prevention were reviewed.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence for Recommendation

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Methods Used to Analyze the Evidence

Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with human immunodeficiency (HIV) infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

*Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection

- Dental Standards of Care Committee
- Mental Health Guidelines Committee
- Committee for the Care of Women with HIV Infection
- Committee for the Care of Substance Users with HIV Infection
- Physicians' Prevention Advisory Committee
- Pharmacy Advisory Committee

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

Evidence Supporting the Recommendations

References Supporting the Recommendations

de Ruiter A, Mercey D, Anderson J, Chakraborty R, Clayden P, Foster G, Gilling-Smith C, Hawkins D, Low-Beer N, Lyall H, O'Shea S, Penn Z, Short J, Smith R, Sonecha S, Tookey P, Wood C, Taylor G. British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women 2008. HIV Med. 2008 Aug;9(7):452-502. PubMed

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Bethesda (MD): Department of Health and Human Services (DHHS); 2011 Oct 14. 167 p.

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. Rockville (MD): Public Health Service Task Force; 2011 Sep 14. 85-7 p. [773 references]

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of patients infected with human immunodeficiency virus type 2 (HIV-2)

Potential Harms

Not stated

Contraindications

Contraindications

Breastfeeding is contraindicated for both human immunodeficiency virus (HIV)-1- and HIV-2-infected mothers, even when receiving antiretroviral therapy.

Qualifying Statements

Qualifying Statements

When formulating guidelines for a disease as complex and fluid as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), it is impossible to anticipate every scenario. It is expected that in specific situations, there will be valid exceptions to the approaches offered in these guidelines and sound reason to deviate from the recommendations provided within.

Implementation of the Guideline

Description of Implementation Strategy

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with human immunodeficiency virus (HIV) infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers, and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative (CEI), the AIDS Educational Training Centers (AETC), and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the New York State Department of Health (NYSDOH) Distribution Center.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the CEI and the AETC. The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-

physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

New York State Department of Health. Human immunodeficiency virus type 2 (HIV-2). New York (NY): New York State Department of Health; 2012 Apr. 14 p. [44 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Apr

Guideline Developer(s)

New York State Department of Health - State/Local Government Agency [U.S.]

Source(s) of Funding

New York State Department of Health

Guideline Committee

Medical Care Criteria Committee

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Financial Disclosures/Conflicts of Interest

Financial disclosures for committee members are available upon request from jciekot@hivguidelines.org.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 15, 2012.

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